REMARKS

Claims 1, 4, 6, 8-10, 14, 16, 18, 20-22, 25-28, 31, 33, 37 and 38 are pending and under examination in the above-identified application. Claims 18 and 20-22, which depended from currently amended claim 14, are cancelled herein as unnecessary in view of claims 6 and 8-10. Nevertheless, Applicants reserve the right to pursue the subject matter of these cancelled claims in a later-filed application claiming the benefit of priority of the above application.

Claims 1, 4, 6, 14, 16, 25-28, 31, 33 and 37 have been amended above. Support for the amendment to claims 1 and 28 can be found, for example, in these claims as originally filed. Claims 4, 6, 14, 16, 25-27, 31, 33, and 37 have been amended to adjust their dependency, conform to the amended base claims, or to correct harmless typographical errors.

Claims 39-50 have been added above. Support for new claims 41, 42, 44, 45, 47, and 48 can be found in claims 1, 14, 28, and 37, as previously presented. Support for new claims 39, 40, 49, and 50, can be found in the Specification as filed at paragraph [055]. Support for new claims 43 and 46 can be found in the Specification as filed at paragraph [031]. Accordingly, the amendments do not raise an issue of new matter and entry thereof is respectfully requested.

Applicants have reviewed the rejections set forth in the Office Action mailed July 18, 2008, and respectfully traverse all grounds for the reasons that follow.

Rejections Under 35 U.S.C. § 103

Claims 1, 4, 6, 8-10, 14, 16, 18, 20-22, 25-28, 31, 33, 37, and 38 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,327,410, (Walt) in view of EP 392 546 A2 (Drmanac). As noted above, claims 18 and 20-22 are canceled above and the rejection is moot as to these claims.

The Office Action alleges that Walt described an array with microspheres, each having analytes from different target sources. However, it is acknowledged that Walt did not specifically exemplify first and second microspheres, each having a plurality of different analytes. As a side issue, Applicants do not agree with the statement that a teaching where "each microsphere has a single type of analyte . . . by definition, encompasses a teaching of

microspheres having more than one type of analyte". For example, while a *claim* reciting "comprising an element" may read on an embodiment having multiple different elements, a claim reciting "more than one type of element" does not read on an embodiment with a single element: there is only one type of element. Here, the claims as amended require "a *plurality of different* target analytes".

Nevertheless, Drmanac is cited as teaching first and second microspheres ("discrete particles" or DPs), each comprising amplification products from genomic DNA, which can serve as bead-bound oligonucleotide probes (ONPs). Because such products would constitute a plurality of different analytes, the Office Action reasons that it would have been obvious to modify the micropheres of Walt by attaching the genomic fragments of Drmanac. The Office Action also states that it would have been obvious to modify the microspheres of Walt with identifier binding ligands as in Drmanac.

Applicants traverse as follows. Drmanac set out to present a comprehensive approach to detecting sequences in genomic DNA, describing obstacles and proposing solutions for overcoming them. For example, Drmanac identified four phases to the approach: sample preparation, probe preparation, hybridization, and reading/storing data. For preparing genomic fragments as probes on DPs, Drmanac defined three possible ways: (1) using genomic fragments, (2) using amplified fragments, and (3) prior enrichment of selected oligonucleotides, of which the first two are cited in the Office Action. The state of the art at the time, however, was problematic for all three, as discussed at col. 13, line 51 to col. 14, line 1:

> The procedure 1. is the most simple one in a technological sense, but the detection of hybridization on a single molecule is a difficult, still unresolved problem. The two other procedures presume many technically untested operations. On the other hand, several different, theoretically possible solution allow conclusion that preparation of defined fragments of genomic DNA, as the separate samples, can be achieved in a DP mix.

To address the unresolved difficulties of detecting single hybridizations for procedure 1, Drmanac explored two problems of "Detection of ONs contents on a level of one DNA molecule" at col. 18, lines 1 to 15:

> If one restricts himself to consideration of hybridization as a procedure for determination of ONs contents, the problem of detection of single target molecule has two components. The first is the possibility . . . of occurrence of the hybridization event with a single target molecule . . . and the second is the detection of the hybrid obtained. Since no efficient or simple procedure for detection of single molecule hybridization has been developed so far, there is no knowledge of this reaction either.

As an alternative to detecting a single hybridization, exponential amplification was considered as a way to enable detection. However, "This [amplification] scheme is just a theoretical possibility in detection of single molecule hybridization and does not presume experimental feasibility." Col. 19, lines 13 to 15. Drmanac concluded with a contrast between the earlier Experimental Approach, and the Informational Approach that it favored:

> The standard method used up to now . . . has two requirements which are almost certainly excluding it as a method of choice. These are the practical impossibility of miniaturization and the need for use of amplified fragments of genomic DNA. The other two methods, which like SBH [sequencing by hybridization] or other procedures using the INFORMATIONAL APPROACH have not been experimentally verified so far, do not impose these requirements. . . . In any case, both procedures are relying on achievements in physics, while INFORMATIONAL APPROACH is exclusively based on biochemical, molecular processes. . . . The entire work in non-informational approach is of the experimental character.

Col. 24, lines 45-55; col. 25, lines 25-26, 48-50. Applicants submit that the untested and theoretical nature of the teaching would have dissuaded a skilled artisan from applying the methods proposed in Drmanac to the microspheres in Walt. While Drmanac may have explored several issues in detecting genomic sequences, the skilled artisan would not have been motivated to amplify fragmented genomic DNA for this purpose, much less amplify from different individuals and separately bind the products from each individual onto their own microspheres, with a reasonable expectation of success at the time. *See* M.P.E.P. § 2143.02 and cases cited therein.

In view of the above, it is respectfully submitted that the combination of Walt and Drmanac cannot render claims 1, 4, 6, 8-10, 14, 16, 18, 20-22, 25-28, 31, 33, 37, and 38 obvious under 35 U.S.C. § 103(a). For the same reasons, Applicants submit that new claims 39-50 would also not be rendered obvious. Therefore, in light of the amendments and remarks, withdrawal of this ground of rejection is respectfully requested.

CONCLUSION

In light of the Amendments and Remarks herein, Applicants submit that the claims are in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, she is invited to call the undersigned attorney.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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